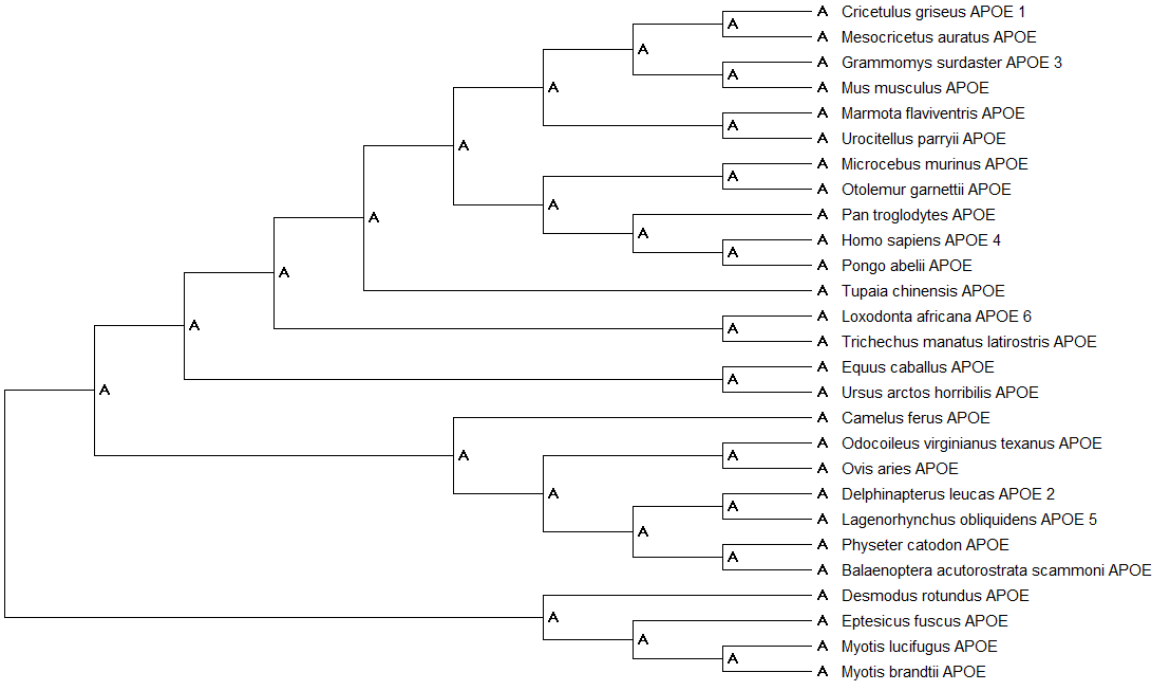
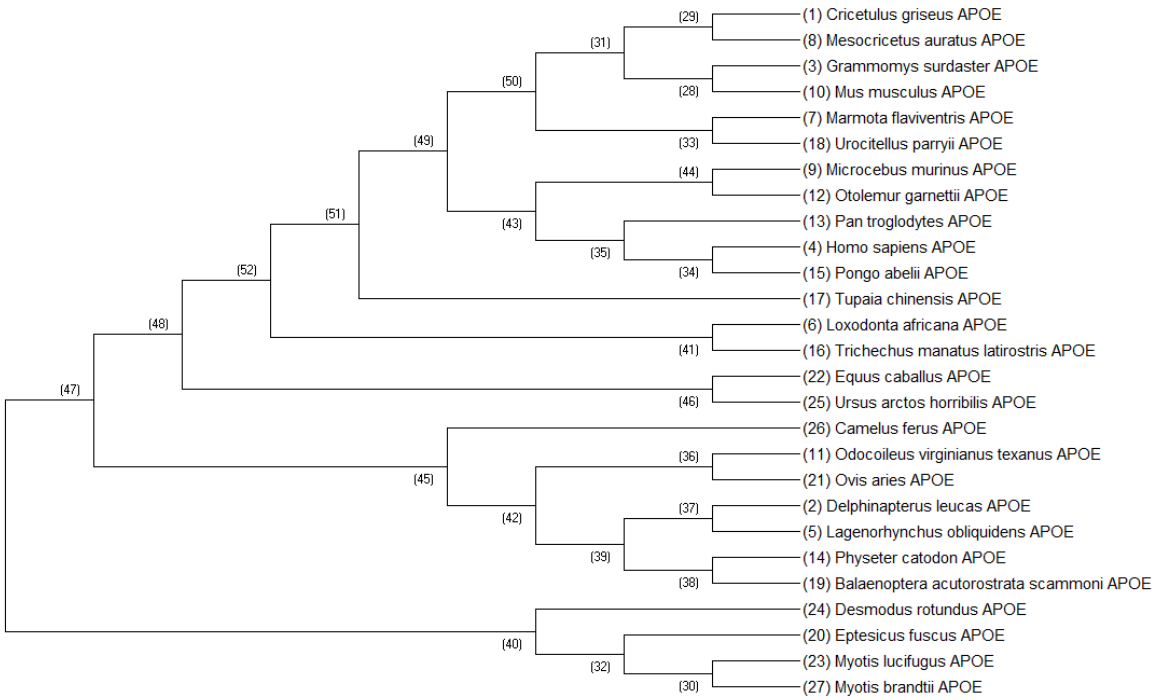
**Part 1**

Reason for finding Ancestral Sequence:

- There have been many recent studies that have shown that primates, strains of mice, humans, cats, and dogs all show signs of Alzheimer's symptoms as well as lesions in post-mortem brains. I am interested to see how far back the APOE gene stretches to determine where there was an evolutionary split in which mammals that we know display symptoms of Alzheimer's; humans, chimpanzees, other primates, etc. and those that we have not observed Alzheimer's symptoms yet.



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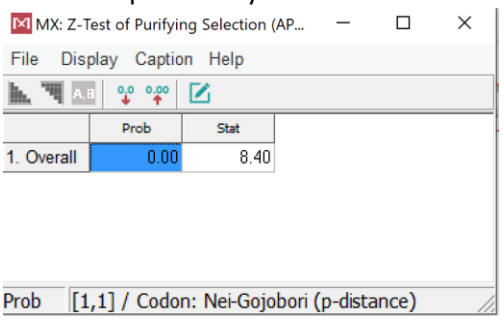
- The nodes of interest that I wanted to look at were (43) and (49). Node (49) is where the split between primates and more closely related rodent species occurred and node (43) is the split between our closely related primate species (pongo abelii, pan trogolodytes) and further related species of otolemur and Microcebus.
    - Node 49 has an accuracy score of 0.9924 and node 43 has an accuracy score is 0.9929.

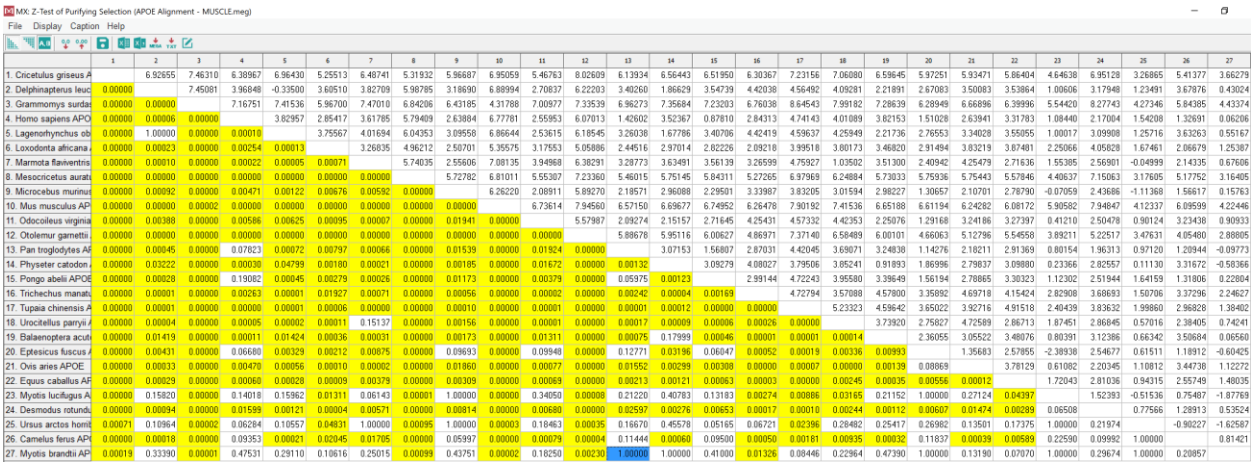
**Part 2**

- The APOE gene is highly important to correct body function as its main function is in lipoprotein-mediated lipid transport between organs through plasma. Of interest, it is extremely important in lipid transport in the CNS, as it helps regulate neuron survival and sprouting. It is also involved in the innate and adaptive immune responses via enabling the survival of myeloid-derived suppressor cells. In a study from 2007, authors B. Maloney, et al. determined that while there is a great deal of homology between the APOE gene in humans and mice, about 180 bp upstream of the TSS displayed only around 40% homology. It is important to note, that mice do NOT naturally display APOE-induced symptoms of Alzheimer's, and that it may be of interest to see how regulatory regions of these genes might actually be the cause of Alzheimer's development in humans and their closely related primate relatives.

**Probability that dN exceeds dS:**

- Accept hypothesis of highly negative selection (reject hypothesis of neutral selection): Probability = 0.00 with a stat pf 8.40
- There is evidence of purifying selection as the probability of the dS exceeding the dN stat by 8.40 has a probability of 0.00.
- 


**Pairwise Comparisons:**

- 


36 of the 221 codons displayed a dN – dS p value of > 0.95, this meaning they are significantly likely to be under purifying selection. There were quite a few on the cusp of being labeled "significantly likely" by

having p-values of near 0.94, but with 0.95 as the cutoff, they were excluded. 16.3% of the codons were significantly likely to be experiencing significant purifying selection. In terms of my sequences, this means that many of the codons are most likely being negatively selected of deleterious codons or mutations.

**Sources:**

https://onlinelibrary.wiley.com/doi/full/10.1111/j.1471-4159.2007.04831.x